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First Named Inventor	Zuker, Charles S.
Art Unit	1649
Examiner Name	Michael T. Brannock
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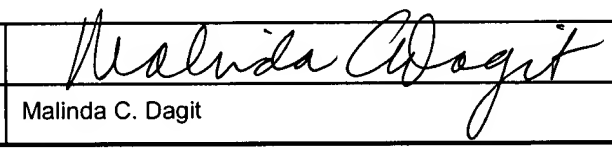
Signature			
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PATENT
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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:	Confirmation No. 5785
Zuker et al.	Examiner: Michael Brannock
Application No.: 09/361,652	Technology Center/Art Unit: 1646
Filed: July 27, 1999	
For: NUCLEIC ACIDS ENCODING A G-PROTEIN COUPLED RECEPTOR INVOLVED IN SENSORY TRANSDUCTION	APPELLANT'S BRIEF UNDER 37 C.F.R. §43.17
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Sir:

This brief is filed in response to the Notice of Non-Compliant Appeal Brief mailed April 11, 2007, and replaces the previous version filed on February 2, 2007.

TABLE OF CONTENTS

I. REAL PARTY IN INTEREST

The real party in interest in U.S. Application No. 09/361,652 is the Regents of the University of California and the National Institutes of Health.

II. RELATED APPEALS AND INTERFERENCES

There are no other pending appeals by Appellants or interferences in which Appellants are involved the outcome of which would directly affect the decision by the Board of Patent Appeals and Interferences in this pending appeal.

III. STATUS OF THE CLAIMS

Claims 1-63 were originally filed. Subsequently, claims 2, 3, 7, 9-33, 36-60 were canceled and claims 64-67 were added. Claims 1, 4-6, 8, 34, 35, and 61-67 are pending in this application. In the final Office Action mailed July 13, 2006, the Examiner rejects all pending claims (1, 4-6, 8, 34, 35, and 61-67) under 35 U.S.C. §101, alleging lack of either a credible specific and substantial utility, or a well-established utility. The Examiner also rejects claims 1, 4-6, 8, 34, 35, and 61-67 under 35 U.S.C. §112, first paragraph, alleging failure to enable the claimed invention based on the utility rejection. Furthermore, the Examiner rejects claims 1, 6, 34, 35, and 61-67 under 35 U.S.C. §112, first paragraph, for alleged inadequate written description. The rejections of claims 1, 4-6, 8, 34, 35, and 61-67 are being appealed.

IV. STATUS OF THE AMENDMENTS

No amendment was filed subsequent to the final Office Action of July 13, 2006.

V. SUMMARY OF CLAIMED SUBJECT MATTER

The claimed subject matter in this appeal relates to a nucleic acid encoding a taste transduction G-protein coupled receptor (GPCR), as well as methods for making an expression vector and a recombinant cell for producing the GPCR recombinantly.

Claim 1

The subject matter claimed in independent claim 1 is an isolated nucleic acid encoding a taste transduction G-protein coupled receptor. The receptor comprises an amino acid sequence having at least 80% identity to SEQ ID NO:1, SEQ ID NO:2, or SEQ ID NO:3, and binds to glutamate, which induces GPCR activity.

Specific support for this claim can be found in the specification, *e.g.*, on page 4, lines 3-6, page 10, lines 24-26, and page 8, lines 8-12, referring to Figure 5.

Claim 61

The subject matter claimed in independent claim 61 is a method of making a taste transduction G-protein coupled receptor. The method comprises the step of expressing the receptor from a recombinant expression vector comprising a nucleic acid encoding the receptor, wherein the receptor comprises an amino acid sequence having at least 80% sequence identity to SEQ ID NO:1, SEQ ID NO:2, or SEQ ID NO:3, and binds glutamate, which induces GPCR activity.

Specific support for this claim can be found in the specification, *e.g.*, on page 6, line 31, to page 7, line 4, page 10, lines 24-26, and page 8, lines 8-12, referring to Figure 5.

Claim 62

The subject matter claimed in independent claim 62 is a method of making a recombinant cell comprising a taste transduction G-protein coupled receptor. The method comprising the step of transducing the cell with an expression vector comprising a nucleic acid encoding the receptor, wherein the receptor comprises an amino acid sequence having at least 80% sequence identity to SEQ ID NO:1, SEQ ID NO:2, or SEQ ID NO:3, and wherein the receptor binds glutamate, which induces GPCR activity.

Specific support for this claim can be found in the specification, *e.g.*, on page 7, lines 5-10, page 10, lines 24-26, and page 8, lines 8-12, referring to Figure 5.

Claim 63

The subject matter claimed in independent claim 63 is a method of making an recombinant expression vector comprising a nucleic acid encoding a taste transduction G-protein coupled receptor. The method comprises the step of ligating to an expression vector a nucleic acid encoding the receptor, wherein the receptor comprises an amino acid sequence having at least 80% sequence identity to SEQ ID NO:1, SEQ ID NO:2, or SEQ ID NO:3, and wherein the receptor binds glutamate, which induces GPCR activity.

Specific support for this claim can be found in the specification, *e.g.*, on page 7, lines 11-16, page 10, lines 24-26, and page 8, lines 8-12, referring to Figure 5.

VI. GROUNDS OF REJECTION TO BE REVIEWED AND APPEALED

1. Claims 1, 4-6, 8, 34, 35, and 61-67 stand rejected for alleged lack of utility.

2. Claims 1, 4-6, 8, 34, 35, and 61-67 stand rejected for alleged lack of enablement.

3. Claims 1, 6, 34, and 61-67 stand rejected for alleged lack of written description.

VII. ARGUMENT

A. The Rejection for Lack of Utility Is Improper

Claims 1, 4-6, 8, 34, 35, and 61-67 stand rejected under 35 U.S.C. §101 because the Examiner alleges that the claimed invention lacks either a well-established utility or a credible specific and substantial asserted utility. Appellants respectfully traverse this rejection and argue that the rejection is improper.

1. Standard to Assess Utility

According to MPEP §2107, the Examiner should review the claims and the supporting written description to determine whether the utility requirement under 35

U.S.C. §101 is met. No rejection based on lack of utility should be made if an invention has a well-established utility, *i.e.*, a utility that will be immediately appreciated by one of ordinary skill in the art based on the characteristics of the invention, regardless any such utility has been asserted. Neither should any rejection be made for lack of utility if an applicant has asserted a specific and substantial utility that would be considered credible by one of ordinary skill in the art.

In most cases, an applicant's assertion of utility creates a presumption of utility that will be sufficient to satisfy the utility requirement of 35 U.S.C. §101. MPEP §2107.02 III A. The Court of Customs and Patent Appeals stated in *In re Langer*:

> As a matter of Patent Office practice, a specification which contains a disclosure of utility which corresponds in scope to the subject matter sought to be patented must be taken as sufficient to satisfy the utility requirement of §101 for the entire claimed subject matter unless there is a reason for one skilled in the art to question the objective truth of the statement of utility or its scope.

In re Langer, 183 USPQ 288, 297 (CCPA, 1974, emphasis in original). To overcome the presumption of sufficient utility as asserted by an applicant, the Examiner must carry the initial burden to make a *prima facie* showing of lack of utility and provide a sufficient evidentiary basis for the conclusion. In other words, the Examiner "must do more than merely question operability--[he] must set forth factual reasons which would lead one skilled in the art to question objective truth of the statement of operability." *In re Gaubert*, 187 USPQ 664, 666 (CCPA 1975).

MPEP §2107.02 IV further states, a detailed explanation should be given for a utility rejection as to why the claimed invention has no specific and substantial asserted utility. Documentary evidence should be provided when possible. Otherwise the Examiner should specifically explain the scientific basis for his factual conclusions.

Moreover, the MPEP states that once the examiner presents a *prima facie* case of unpatentability for lack of utility, the burden of coming forth with evidence or arguments shifts to the applicant. After evidence or argument is submitted by the

applicant in response, patentability is determined on the totality of the record and by a preponderance of evidence with due consideration to persuasiveness of argument. "If the record as a whole would make it more likely than not that the asserted utility for the claimed invention would be considered credible by a person of ordinary skill in the art, the Office cannot maintain the rejection." MPEP §2107.02 VI.

2. The Asserted Utility and the Examiner's Rejection

The present invention relates to the identification of G-protein coupled receptor (GPCR) B3, a GPCR expressed specifically in taste cells. It is asserted in the specification that this taste cell specific GPCR is a component of the taste signal transduction pathway and is capable of, via its interaction with a G-protein, mediating taste (such as sweet, bitter, unami, *etc.*) perception. *See, e.g.*, page 3, lines 7-10; page 3, line 31, to page 4, line 2; and page 9, lines 30-33, of the specification. It is further asserted that GPCR-B3 polypeptides or the encoding nucleic acids can be used, for example, as probes to identify taste cells, to generate taste topographic map, and to provide a screening method for compounds that can modulate taste signaling and are therefore useful in the food and pharmaceutical industries. *See, e.g.*, page 8, line 16, to page 9, line 10, of the specification.

In addition, Appellants previously submitted Dr. Zuker's declaration under 37 C.F.R. §1.132 (along with Appellants' response of September 16, 2002). In this declaration, Dr. Zuker attests that given the structure and expression pattern of GPCR-B3, as well as the results of a functional assay using a chimeric GPCR construct, one of skill in the art would readily recognize, at the time this application was filed, the immediately available of use of the claimed GPCR-B3 polynucleotides or polypeptides, *e.g.*, for identifying modulators of taste signal transduction. It is therefore established that an ordinarily skilled artisan would find the asserted utility specific, substantial, and credible.

In several previous Office Actions as well as the July 13, 2006, final Office Action, the Examiner takes the position that the GPRC-B3 polypeptide lacks substantial utility, or a "real world" use, because the polypeptide is not described as to be involved in any particular aspect of the taste perception. In response, Appellants cited in their response of October 23, 2003, the reference by Nelson *et al.* (attached as Appendix 2 of this brief, previously made of record as reference BE in the IDS filed September 16, 2002), which shows that GPCR-B3 (also known as T1R1), forming a heterodimeric GPCR with T1R3 and functioning as an L-amino acid taste receptor, is indeed involved in a definitive aspect of the taste perception. In the previous Office Actions and the July 13, 2006, final Office Action, however, the Examiner continues to disagree with Appellants' position that the Nelson *et al.* reference supports a finding of patentable utility, stating that since the presence of GPCR-B3 in this heterodimeric receptor is described only in this reference but not in the present specification, one of skill in the art would not recognize or believe such use of GPCR-B3 after reading the specification.

3. The Examiner Has Raised and Maintained the Utility Rejection in a Manner Inconsistent with the MPEP

Appellants have asserted a specific and substantial utility in the specification and submitted Dr. Zuker's declaration to demonstrate that this asserted utility is credible to one of skill in the art. In contrast, the Examiner has not provided any evidence or objective reason to overcome the presumed patentable utility. The Nelson *et al.* reference was provided merely as an example of confirmed involvement of GPCR-B3 in taste signaling. On the other hand, it is possible that GPCR-B3 can act alone or in complex with other proteins including other GPCRs to mediate taste signal transduction. The Nelson reference was not cited by any means to indicate or suggest that GPCR-B3's sole involvement in taste perception is via complexing with T1R3 to form a heterodimer. This reference was cited to demonstrate the credibility of the asserted utility that GPCR-B3 is involved in taste signaling and is therefore useful in, *e.g.*, screening methods for identifying taste-modulating compounds. Thus, whether or not the specification

describes this particular heterodimer of GPCR-B3 and T1R3 is not directly relevant to whether one of skill in the art would find the asserted utility credible. In fact, the notion that one of skill in the art would, at the time this application was filed, find the asserted utility (which is not limited to the heterodimer of GPCR-B3 and T1R3) credible has already been established by Dr. Zuker's declaration and not yet rebutted by the Examiner.

Raising and maintaining a rejection for lack of utility in such a manner is inconsistent with the proper practice described in the MPEP, which places the initial burden on the Examiner, not Appellants, to provide evidence to support a factual conclusion of the credibility of an asserted utility. In fact, MPEP §2107.02 III.B. specifically cautions Office personnel that, once an assertion of a particular utility is made, "that assertion cannot simply be dismissed ..... as 'wrong,' even when there may be reason to believe the assertion is not entirely accurate." Instead, the Examiner must provide an explanation setting forth the reasoning used in concluding that the asserted specific and substantial utility is not credible; support for factual findings relied upon in reaching the conclusion; and an evaluation of all relevant evidence of record, including utilities taught in the closest prior art. MPEP §2107.02 IV. Furthermore, it is stated in MPEP §2107.02 VI that, after the Examiner has provided evidence or objective reasons to question the credibility of an asserted utility, and the applicant has further responded with evidence or argument, "patentability is determined on the totality of the record, by a preponderance of evidence with due consideration to persuasiveness of argument." A utility rejection cannot be properly maintained if the record as a whole indicates it is more likely than not that one of skill in the art would consider the asserted utility credible.

In the present case, Appellants have responded to the Examiner's questioning of the asserted utility by offering Dr. Zuker's declaration, which establishes that one of skill in the art would reasonably believe the asserted utility, as well as the Nelson *et al.* reference, which provides an example of GPCR-B3's involvement in taste signaling; on the other hand, the Examiner has offered no evidence or objective reasons

why the asserted utility is not credible. Indeed, in the final Office Action of July 13, 2006, the Examiner again rejects the Appellants' assertion of utility, particular the assertion that GPCR-B3 alone can act alone or in complex with other proteins to mediate taste signaling, stating that "[m]any things are possible but simply inviting an artisan to test various ideas to try to find a way to use the polypeptide does not provide for a substantial utility" (the first full paragraph on page 3 of the final Office Action). Offering no evidence or objective reasons to contradict the asserted utility, the Examiner's statements merely reflect his personal disbelief of the asserted utility, which is supported by both Dr. Zuker's declaration and the Nelson reference.

Appellants thus submit that when considered together, the record favors a holding of sufficient credibility in the asserted utility.

4. Summary

Appellants do not believe that the Examiner has adhered to the proper standards for assessing utility as described in the MPEP. The utility rejection is therefore improper and should be withdrawn.

B. The Rejection for Inadequate Enablement Based on Utility Is Improper

The Examiner has also maintained the rejection of claims 1, 4-6, 34, 35, and 61-67 on enablement ground, alleging that the claimed invention is not supported by either a credible specific and substantial asserted utility or a well-established utility. As discussed above, the claimed invention has a credible specific and substantial utility. Appellants therefore believe that the enablement rejection under 35 U.S.C. §112, first paragraph, is improper and should be withdrawn.

C. The Rejection for Inadequate Written Description Is Improper

The Examiner has further rejected claims 1, 6, 34, 35, and 61-67 under 35 U.S.C. §112, first paragraph, alleging that the claimed invention is not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that

the inventor, at the time the application was filed, had possession of the claimed invention.

As will be discussed in detail below, the claimed invention as described in the present application fully complies with the requirement for written description as set forth by the MPEP and prevailing case law. Appellants thus submit that the written description rejection is improper and should be withdrawn.

1. Standard for Written Description

According to the MPEP, to satisfy the written description requirement, a patent specification must describe the claimed invention in sufficient detail such that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention. Possession of a claimed invention may be demonstrated by description of the invention with all of its limitations using such descriptive means as words, structures, figures, diagrams, and formulas that fully set forth the claimed invention. MPEP §2163 I. Moreover, a strong presumption exists with regard to originally filed claims that an adequate written description of the claimed invention is present when the application is filed. MPEP §2163 I.A.

Case law indicates that structural features of a claimed invention are important for satisfying the written description requirement. The Federal Circuit in *Fiers v. Revel*, 25 USPQ2d 1601 (Fed. Cir. 1993), stated that an adequate written description "requires a precise definition, such as by structure, formula, chemical name, or physical properties." *Fiers*, 25 USPQ2d at 1606. The requirement for written description of a chemical genus is further set forth in *University of California v. Eli Lilly & Co.*, 43 USPQ2d 1398 (Fed. Cir. 1997). As described by the Federal Circuit in *Lilly*, "[a] description of a genus of cDNAs may be achieved by means of . . . a recitation of structural features common to the members of the genus . . . ." *Lilly*, 43 USPQ2d at 1406.

Moreover, proper description of functional features of a claimed invention can also satisfy the written description requirement. In *Enzo Biochem, Inc. v. Gen-Probe Incorporated*, 63 USPQ2d 1609 (Fed. Cir. 2002), the claimed polynucleotide sequences in the patent in question are defined based on their ability to differentially hybridize to reference polynucleotide sequences from deposited bacteria *N. gonorrhoeae* and *N. meningitidis*. The Federal Circuit held that this hybridization function-based description may, in some cases, satisfy the written description requirement because of "a complementary structural relationship" between the claimed sequences and the reference sequences. *Enzo*, 63 USPQ2d at 1616. The Federal Circuit further stated that "*Lilly* did not hold that all functional descriptions of genetic material necessarily fail as a matter of law to meet the written description requirement; rather, the requirement may be satisfied if in the knowledge of the art the disclosed function is sufficiently correlated to a particular, known structure." *Amgen Inc. v. Hoechst Marion Roussel Inc.*, 65 USPQ2d 1385, 1398 (Fed. Cir. 2003).

2. The Claimed Invention Is Defined by Its Structural and Functional Features

The present invention relates to the identification of nucleic acids encoding a novel G-protein coupled receptor, GPCR-B3. It is Appellants' intent to include in the claim scope nucleic acids encoding allelic variants and man-made muteins that retain the polypeptide's normal function. For example, the specification states that polymorphic variants of rat GPCR-B3 (SEQ ID NO:1) are a part of the invention and provides three substitution variants, *e.g.*, isoleucine substituted by leucine at position 33, aspartic acid substituted by glutamic acid at position 84, and glycine substituted by alanine at position 90 (page 10, lines 11-16, of the specification). The claimed nucleic acids are defined by their shared structural features, *i.e.*, they encode polypeptides with at least 80% amino acid sequence identity to the sequence disclosed in SEQ ID NO:1, SEQ ID NO:2, or SEQ ID NO:3.

Percent amino acid sequence identity of a polypeptide to a reference amino acid sequence is a structural property of the polypeptide, because such percent identity relies entirely upon the polypeptide's amino acid sequence. This structural attribute of the polypeptide is in turn a structural attribute of the nucleic acid encoding the polypeptide, since the amino acid sequence is determined by the polynucleotide sequence of an encoding nucleic acid. Moreover, the recitation of an amino acid sequence identity makes identification of the polypeptides and thus the claimed nucleic acids easily accomplished by one of skill in the art. Algorithms for determining percent sequence identity and sequence similarity for the identification of polypeptides and their coding polynucleotide sequences are well known to those of skill in molecular biology and are described in the present specification on pages 19 to 22. The present claims can be analogized with *Fiers*, *Lilly*, and *Enzo* in that they all relate to genetic material. The description of the claimed nucleic acids relies on a percentage sequence identity to a reference sequence and thus establishes a structural feature in a manner even more direct than that in the *Enzo* case.

The claimed nucleic acids are also defined by shared functional features, *i.e.*, they encode polypeptides that are G-protein coupled receptors and bind to glutamate, which induces the GPCR activity. The specification provides functional assays for identifying the polypeptides with such functional features. On page 41, line 27, to page 47, line 10, for instance, the specification teaches isolating a putative GPCR-B3 polypeptide or expressing the polypeptide in a cell, and examining whether the polypeptide is a GPCR protein demonstrating the characteristic GPCR activity, particularly upon binding to a ligand (*e.g.*, glutamate). These assays are used to confirm that a putative GPCR-B3 polypeptide is actually a GPCR polypeptide within the claim scope by examining the polypeptide's physical or chemical effects. The specification further teaches that to demonstrate the GPCR activity, a candidate polypeptide, either naturally occurring or recombinantly produced, can be studied *in vivo* or *in vitro*, when the polypeptide is isolated, expressed in a cell, expressed in a membrane derived from a

cell, or expressed in a tissue or in an animal (page 42, lines 13-24). These assays thus allow one skilled in the art to identify the claimed nucleic acids based on the functional attributes of the polypeptides they encode.

Thus, both structural and functional features commonly shared by all members of the claimed genus of GPCR-B3 nucleic acids have been described in detail, which "clearly allow persons of ordinary skill in the art to recognize that [the applicant] invented what is claimed." *Vas-Cath Inc. v. Mahurkar*, 19 USPQ2d 1111, 1116 (Fed. Cir. 1991). This description of the claimed invention is consistent with the holdings of *Lilly*, *Enzo*, and *Amgen*.

In sustaining the claim rejection for alleged inadequate written description, the Examiner contends that the specification does not provide a correlation between any particular structure of the GPCR-B3 polypeptide encoded by the claimed nucleic acid and any particular function, and that reciting a percent sequence identity to a reference sequence does not provide any particular common structure or the information regarding the particular amino acid residues that are important to the GPCR-B3 polypeptide function (the first full paragraph on page 5 of the final Office Action mailed July 13, 2006). Appellants cannot agree with the Examiner.

As discussed above, sequence similarity is a structural feature of a polypeptide and its coding polynucleotide sequence. At the time this application was filed, the inventors clearly had possession of three naturally occurring GPCR-B3 amino acid sequences from rat, mouse, and human (SEQ ID NO:1, SEQ ID NO:2, and SEQ ID NO:3, respectively). Relying on sequence alignment and analysis using methods well known to those of skill in the art or methods taught in the present disclosure, an artisan would be able to readily determine whether certain amino acid residues in these proteins are likely to be critical for the protein's functionality, depending on whether these residues are conserved among the three GPCR proteins as well as other known GPCR proteins. Based on this determination, an artisan would be able to derive a large number

of amino acid sequences (and their coding polynucleotide sequences) as putative GPCR-B3 polypeptides, which can then be examined for the required functionality according to the methods known in the art or described in the specification. When all these factors are considered, Appellants contend that the three exemplary GPCR-B3 polypeptide sequences not only illustrate their common structural feature but together also provide a reasonably degree of sequence variation in their common structural feature, which is directly tied to the GPCR activity.

3. Summary

Appellants believe that the written description rejection under 35 U.S.C. §112 is improper and should be withdrawn.

VIII. CONCLUSION

In view of the foregoing, Appellants believe all claims now pending in this Application are in condition for allowance.

Respectfully submitted,

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IX. CLAIMS APPENDIX

1. An isolated nucleic acid encoding a taste transduction G-protein coupled receptor, wherein the receptor comprises an amino acid sequence having at least 80% identity to SEQ ID NO:1, SEQ ID NO:2, or SEQ ID NO:3, and wherein the receptor binds to glutamate, which induces GPCR activity.

4. The isolated nucleic acid of claim 1, wherein the nucleic acid encodes a receptor comprising an amino acid sequence of SEQ ID NO:1, SEQ ID NO:2, or SEQ ID NO:3.

5. The isolated nucleic acid sequence of claim 1, wherein the nucleic acid comprises a nucleotide sequence of SEQ ID NO:4, SEQ ID NO:5, or SEQ ID NO:6.

6. The isolated nucleic acid of claim 1, wherein the nucleic acid is from a human, a mouse, or a rat.

8. The isolated nucleic acid of claim 1, wherein the nucleic acid encodes a receptor having a molecular weight of about between 92 kDa to about 102 kDa.

34. An expression vector comprising the nucleic acid of claim 1.

35. A host cell transfected with the vector of claim 34.

61. A method of making a taste transduction G-protein coupled receptor, the method comprising the step of expressing the receptor from a recombinant expression vector comprising a nucleic acid encoding the receptor, wherein the receptor comprises an amino acid sequence having at least 80% sequence identity to SEQ ID NO:1, SEQ ID NO:2, or SEQ ID NO:3, and wherein the receptor binds glutamate, which induces GPCR activity.

62. A method of making a recombinant cell comprising a taste transduction G-protein coupled receptor, the method comprising the step of transducing the cell with an expression vector comprising a nucleic acid encoding the receptor, wherein the receptor comprises an amino acid sequence having at least 80% sequence identity to SEQ ID NO:1, SEQ ID NO:2, or SEQ ID NO:3, and wherein the receptor binds glutamate, which induces GPCR activity.

63. A method of making an recombinant expression vector comprising a nucleic acid encoding a taste transduction G-protein coupled receptor, the method comprising the step of ligating to an expression vector a nucleic acid encoding the receptor, wherein the receptor comprises an amino acid sequence having at least 80% sequence identity to SEQ ID NO:1, SEQ ID NO:2, or SEQ ID NO:3, and wherein the receptor binds glutamate, which induces GPCR activity.

64. The nucleic acid of claim 1, wherein the receptor comprises an amino acid sequence have at least 90% sequence identity to SEQ ID NO:1, SEQ ID NO:2, or SEQ ID NO:3.

65. The method of claim 61, wherein the receptor comprises an amino acid sequence have at least 90% sequence identity to SEQ ID NO:1, SEQ ID NO:2, or SEQ ID NO:3.

66. The method of claim 62, wherein the receptor comprises an amino acid sequence have at least 90% sequence identity to SEQ ID NO:1, SEQ ID NO:2, or SEQ ID NO:3.

67. The method of claim 63, wherein the receptor comprises an amino acid sequence have at least 90% sequence identity to SEQ ID NO:1, SEQ ID NO:2, or SEQ ID NO:3.

X. EVIDENCE APPENDIX

1. Declaration under 37 C.F.R. §1.132 by Dr. Charles Zuker. Submitted September 16, 2004

2. Nelson *et al.*, *Nature*, advance online publication, Feb. 24, 2002 (DOI 10.1038/nature726). Submitted as reference BE in IDS filed September 16, 2004.

XI. RELATED PROCEEDINGS APPENDIX

None.

X. EVIDENCE APPENDIX

1. Zuker Declaration